TNX- 355

Drug Class: **Entry and Fusion Inhibitors**

Drug Description

TNX-355 is a nonimmunosuppressive, humanized IgG4, anti-CD4, domain 2 monoclonal antibody that prevents HIV entry into human cells. [1] [2]

HIV/AIDS-Related Uses

TNX-355 is being investigated in Phase II trials as part of combination therapy for the treatment of HIV-1 infection in treatment-experienced patients.[3] The manufacturer was awarded fast track status for TNX-355 development by the FDA in October 2003.[4]

Pharmacology

TNX-355 inhibits HIV entry into lymphocytes and binds to an epitope in domain 2 of the CD4 receptor on a cell's surface, preventing HIV entry into the cell.[5] TNX-355 does not deplete CD4. Unlike anti-CD4 antibodies that target domain 1 of CD4, TNX-355 does not appear to interfere with immunologic functions involving antigen presentation and is not immunosuppressive.[6] [7]

A Phase Ia study evaluated single 0.3 to 25 mg/kg doses of TNX-355; these doses reduced viral load from baseline by 50% to 90%. This effect was transient, with most levels returning to baseline by Day 28. Significant viral load reductions were observed with the 10 and 25 mg/kg doses and were sustained for 2 to 3 weeks.[8] [9]

In a Phase Ib study, 23% of patients had reduced viral loads by greater than 95%, and 64% had reduced loads by greater than 90%. However, these reductions were also transient, implying that monotherapy may cause quick development of resistance.[10]

An ongoing Phase II, 48-week, multicenter, randomized, double-blind, placebo-controlled trial is comparing two doses of TNX-355 or placebo when added to optimized background therapy in HIV patients who have failed or are failing highly active antiretroviral therapy (HAART).[11] The study will evaluate virologic failure rates and compare viral load reduction between the two doses and between each dose and placebo at 24 weeks.[12] Enrolled patients must have a viral load of 10,000 copies/ml or greater, a CD4 count greater than 50 cells/ml, and triple-class experience with HAART. Patients will receive one IV infusion of TNX-355 or placebo weekly for 8 weeks, then one infusion twice weekly.[13]

TNX-355 has potential advantages over currently available HIV therapies due to the low risk of cross resistance.[14]

Adverse Events/Toxicity

In Phase Ia and Ib safety studies, TNX-355 was well tolerated. No serious adverse effects were reported in the Phase Ia study. Depression recurrence, vasovagal reaction with new onset seizure, and acute renal failure with renal insufficiency were reported in three patients in a Phase Ib, 22-patient study.[15] [16]

Drug and Food Interactions

The manufacturer reports possible synergy of TNX-355 with enfuvirtide in vitro.[17]

Clinical Trials

For information on clinical trials that involve TNX-355, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: TNX-355 AND HIV Infections.

Dosing Information

Mode of Delivery: Intravenous.[18]

Dosage Form: In clinical trials, TNX-355 has been given intravenously once weekly or twice monthly. Doses evaluated include 6, 10, 15, and 25 mg/kg.[19] [20]

Other Names

Hu5A8[21]

Further Reading

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Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

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